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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/368,010	08/03/99	KASPER K	BEH-7443

EXAMINER	
CEPERLEY, M	
ART UNIT	PAPER NUMBER
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DADE BEHRING INC.
1717 DEERFIELD ROAD, #778
ATTN: LOIS K. RUSZALA
DEERFIELD IL 60015-0778

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/368,010	Applicant(s) KASPER ET AL.	
	Examiner Mary E. (Molly) Ceperley	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) *1-10, 13-30, 34-49, 52-60, and 62-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 12, 31-33, 50, 51, and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

1. Claims 1-10, 13-30, 34-49, 52-60, and 62-82 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicants timely traversed the restriction (election) requirement of November 01, 000 (Paper No. 4) in their response of December 28, 2000 (Paper No. 5). Claims 11, 12, 31-33, 50, 51 and 61 have been examined on the merits in this Office action.

Applicants note in their response of December 28, 2000 that a facsimile restriction requirement had been previously sent by the examiner which indicated a different grouping of claims than that set forth in the official written restriction requirement of November 01, 2000. However, the ***written*** restriction of November 01, 2000 still stands in view of the fact that *(1)* a facsimile response by applicants to the original facsimile requirement was not of record in the application and *(2)* upon further consideration of the claimed subject matter, the examiner concluded that, in fact, multiple distinct inventions are claimed as set forth in the groupings of the written restriction requirement of November 01, 2000.

In their December 28, 2000 response applicants argue that Groups I-XIV are not distinct. For example, applicants argue that the Groups V and VI are not distinct i.e. that the same inventive concept is involved for Group V wherein tacrolimus is derivatized with a carboxymethyl oxime moiety at a carbon atom in the non-binding domain as it is for Group VI which specifies that derivatization is with an oxime moiety at carbon atom 22. However, these groups are considered to be distinct for the reason that between the two groups both *different* derivatization agents *and different* points of attachment of the immunogenic carrier are involved. It is also noted that although applicants may consider Group IV to be a subset of Group III, for example, claim 11 is not dependent from claim 10 and the scope of the term "a carbon atom in

the non-binding domain" of claim 10 is different than the scope of the term "carbon 22" of claim 11. The considerations for making a patentability determination of a monoclonal antibody based on the limitations of claim 1 of Group I (i.e. binding affinity of 3.7×10^9 liters/mole, < 8% cross-reactivity to specific metabolites, and specific MAb designation), for example, ***would be clearly different from*** the considerations involved in determining the patentability of a monoclonal antibody defined by the characteristics of claim 11 of Group IV (i.e. immunogenic carrier derivatization with carboxymethyl oxime at carbon atom 22 with no definitions of either binding affinity or cross-reactivity). A reference which might anticipate the monoclonal antibodies of Group IV would not necessarily render obvious the monoclonal antibody of Group I.

For the above reasons the written restriction requirement of record is made FINAL.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 11, 12, 13-33, 50, 51, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the "monoclonal antibody" of claim 11 ***is produced from the hybridoma*** which is produced by the method steps recited in claim 11. This rejection could be overcome by inserting in claim 11, line one, after the word "by", the words ---a hybridoma produced by--- .

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 11, 12, 31-33, 50, 51 and 61 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over each of Niwa et al (U.S. 5,532,137), Fujisawa Pharm. Co. (WO 94/04700), Jeong et al (Abstract: 6th Internat'l. Congress of TDM-CT), Grenier et al (U.S. 5,635,406), or Backman et al (Transplantation, 57 (4): 519-525 (1994)).

Claim 11 is a product-by-process claim drawn to a monoclonal antibody with specificity for tacrolimus which appears to be the same as or functionally equivalent to the monoclonal antibodies described in the prior art. See Niwa et al: Examples 1 and 4; Fujisawa Pharm. Co.: abstract; Jeong et al: antibody against FK506; Grenier et al: col. 3, lines 31-39 and Example 1; Backman et al: page 520, *FK506 determination methodology*. As a product-by-process claim, claim 11 is properly rejected under either 35 USC 102 or 103 in accordance with the practice set forth in MPEP 2113. Further in accordance with this practice, the burden is shifted to applicants

to show an unobvious difference between the monoclonal antibodies of the instant invention and those of the prior art.

It is noted that Examples 6, 8 and 9 of the instant application provide comparisons among various monoclonal tacrolimus antibodies which might possibly be used to establish a difference between the claimed monoclonal antibodies and those of the prior art. However, it is not clear as to which specific hapten was conjugated to which specific immunogenic carrier to prepare each tested antibody. For example, it is not clear if Example 2 prepares the *carbon-22* substituted immunogen used in claim 11 or how antibody 14H04 of Example 6 is prepared. Applicants should point out the differences in hapten structures used to prepare the immunogens and differences in specificity/cross-reactivity among the various antibodies which are evaluated in the working examples of the specification.

The use of monoclonal antibodies in conventional immunoassays for tacrolimus (instant claim 50) are described by the prior art references in the sections of the references cited above. The packaging of test components in kit form (claim 61) is a well known expedient for convenience in immunoassay performance. See also, the test kits of claims 7-13 of Niwa et al.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. (Molly) Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-7230.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Mary E. Ceperley

Mary E. Ceperley
Primary Examiner
Art Unit 1641